

manufacture of a medicament for the treatment or prophylaxis of diseases or conditions of mammals.

17. (Once Amended) A composition comprising a cyclic conotoxin peptide according to claim 1 and a pharmaceutically acceptable carrier or diluent.

### REMARKS

The Office Action mailed on July 26, 2002 requires that Applicants select one peptide linker in claim 9 and one cyclic conotoxin peptide in claim 10. In response, Applicants elect SEQ ID NO:2 as the peptide linker in claim 9 and SEQ ID NO:6 as the cyclic peptide in claim 10.

This election, however, is made with traverse because the Office Action fails to demonstrate adequate basis for restriction. When restricting claims due to alleged lack of unity, the Examiner must (1) list the different group of claims, and (2) explain why each group lacks unity with each other group specifically describing the unique special technical feature in each group. A group of inventions is considered linked to form a general inventive concept where there is a technical relationship among the inventions that involves at least one common or corresponding special technical feature. The expression special technical feature is defined as meaning those technical features that define the contribution which each claimed invention, considered as a whole, makes over the prior art. MPEP 1893.03(d).

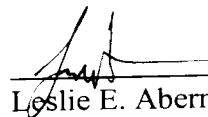
The outstanding Office Action mistakenly asserts that the pending claims do not involve a common special technical feature. Before the advent of the present invention, conotoxin peptides were known to be linear in form, having free N or C termini. The present Applicants were the first to appreciate that the properties of a conotoxin peptide can be

improved by joining the N and C termini to produce a non-linear cyclised conotoxin peptide. Accordingly, the invention involves, in part, the discovery that the cyclisation of a conotoxin peptide is both possible and desirable. The common technical feature present throughout the claims is the cyclisation of a conotoxin peptide.

Applicants have amended the claims to even more clearly reflect the nature of the invention and more distinctly point out the common technical feature present throughout the claims – the cyclisation of a conotoxin peptide. Accordingly, Applicants believe that the requirement to elect a specific peptide linker from claim 9 and cyclic conotoxin peptide from claim 10 is improper and respectfully request that the restriction be withdrawn.

The claims presently before the Examiner are believed to patentably define the invention over the prior art and otherwise be in condition for allowance. An early Office Action to that effect, is therefore, earnestly solicited.

Date: Jan 17, 2003

  
\_\_\_\_\_  
Leslie E. Aberman  
Limited Recognition Under 37 CFR §  
10.9(b) attached

Woodcock Washburn LLP  
One Liberty Place - 46th Floor  
Philadelphia PA 19103  
Telephone: (215) 568-3100  
Facsimile: (215) 568-3439

APPENDIX AVERSION WITH MARKINGS TO SHOW CHANGES MADE

1. (Once Amended) A cyclised conotoxin peptide having no free N- or C-termini.
2. (Once Amended) A cyclised conotoxin peptide according to claim 1 having an activity associated with the therapeutic treatment of mammals.
3. (Once Amended) A cyclic conotoxin peptide according to claim 1 which contains or consists of the sequence of amino acids present in a naturally occurring conotoxin peptide or derivative thereof.
5. (Once Amended) A cyclic conotoxin peptide according to claim 1 having three disulphide bonds in the form of a cysteine knot.
6. (Once Amended) A cyclic conotoxin peptide according to claim 1 comprising a linear conotoxin peptide and a peptide linker, wherein the N- and C- termini of the linear peptide are linked via the peptide linker to form an amide cyclised peptide backbone.
10. (Once Amended) A cyclic conotoxin peptide according to claim 1 selected from the group consisting of:

CKGKGAKCSRLMYDCCTGSCRSKGKCTRNLPG SEQ. ID NO. 5

CKGKGAKCSRLMYDCCTGSCRSGKCTRNG

SEQ. ID NO. 6

GLPVCKGKGAKCSRLMYDCCTGSCRSGKCTRNG

SEQ ID NO. 7

GCCSNPVCHLEHSNLCTNG

SEQ ID NO. 8

CCSNPVCHLEHSNLCTNGG

SEQ ID NO. 9

11. (Once Amended) A process for preparing a cyclic conotoxin according to claim 1 comprising:

(i) synthesizing an extended linear conotoxin peptide on a solid phase support, said extended linear conotoxin peptide comprising a linear conotoxin peptide having a linker moiety attached to at least one end thereof,

(ii) cleaving said extended linear peptide from the support

(iii) cyclising said extended linear conotoxin peptide, and

(iv) oxidizing said cyclised peptide to form disulphide bonds.

12. (Once Amended) A process for preparing a cyclic conotoxin according to claim 1 comprising:

(i) synthesizing an extended linear conotoxin peptide on a solid phase support, said extended linear conotoxin peptide comprising a linear conotoxin peptide having a linker moiety attached to at least one end thereof,

(ii) cleaving said linear peptide from the solid support,

(iii) subjecting said extended peptide to conditions such that the peptide folds and forms the required disulphide bonds, and

(iv) cyclising the folded peptide.

13. (Once Amended) A process for preparing a cyclic conotoxin according to claim 1 comprising:

- (i) reacting a conotoxin peptide with a linker moiety to form an extended linear conotoxin peptide having said linker moiety attached to one end thereof, and
- (ii) cyclising said extended peptide and oxidizing to form disulphide bonds, if required.

14. (Once Amended) Use of a cyclic conotoxin peptide according to claim 1 having activity at ion channel receptors as a neuropharmacological probe.

15. (Once Amended) A method for the treatment or prophylaxis of conditions or diseases in mammals including the step of administering a cyclic conotoxin peptide according to claim 1.

16. (Once Amended) Use of a cyclic conotoxin peptide according to claim 1 in the manufacture of a medicament for the treatment or prophylaxis of diseases or conditions of mammals.

17. (Once Amended) A composition comprising a cyclic conotoxin peptide according to claim 1 and a pharmaceutically acceptable carrier or diluent.

**APPENDIX B****PENDING CLAIMS SUBJECT TO EXAMINATION**

1. (Once Amended) A cyclised conotoxin peptide having no free N- or C-termini.
2. (Once Amended) A cyclised conotoxin peptide according to claim 1 having an activity associated with the therapeutic treatment of mammals.
3. (Once Amended) A cyclic conotoxin peptide according to claim 1 which contains or consists of the sequence of amino acids present in a naturally occurring conotoxin peptide or derivative thereof.
4. A cyclic conotoxin peptide according to claim 3 wherein the naturally occurring conotoxin peptide is selected from MVIA, GVIA, SVIB, SVIA, TVIA, MVIIC, GVIIA, GVIIIB, PVIIA, GS, GI, IMI, PNIA, PNIB, SII, MII, GIIIA, GIIIB, GIIC and PIIIA.
5. (Once Amended) A cyclic conotoxin peptide according to claim 1 having three disulphide bonds in the form of a cysteine knot.
6. (Once Amended) A cyclic conotoxin peptide according to claim 1 comprising a linear conotoxin peptide and a peptide linker, wherein the N- and C- termini of the linear peptide are linked via the peptide linker to form an amide cyclised peptide backbone.

7. A cyclic conotoxin peptide according to claim 6 wherein the linear conotoxin peptide moiety is derived from a naturally occurring conotoxin peptide and retains the disulphide bond connectivity of the naturally occurring conotoxin peptide.

8. A cyclic conotoxin peptide according to claim 6 wherein the peptide linker is from 2 to 15 amino acids in length.

9. A cyclic conotoxin peptide according to claim 6 wherein the peptide linker is selected from the group consisting of:

TRNGLPG SEQ ID NO. 1

TRNG SEQ ID NO. 2

TRGGLPV SEQ ID NO. 3

TNG SEQ ID NO. 4

10. (Once Amended) A cyclic conotoxin peptide according to claim 1 selected from the group consisting of:

CKGKGAKCSRLMYDCCTGSCRSGKCTRNGLPG SEQ. ID NO. 5

CKGKGAKCSRLMYDCCTGSCRSGKCTRNG SEQ. ID NO. 6

GLPVCKGKGAKCSRLMYDCCTGSCRSGKCTRG SEQ ID NO. 7

GCCSNPVCHLEHSNLCTNG SEQ ID NO. 8

CCSNPVCHLEHSNLCTNGG SEQ ID NO. 9

11. (Once Amended) A process for preparing a cyclic conotoxin according to claim 1 comprising:

(i) synthesizing an extended linear conotoxin peptide on a solid phase support, said extended linear conotoxin peptide comprising a linear conotoxin peptide having a linker moiety attached to at least one end thereof,

(ii) cleaving said extended linear peptide from the support

(iii) cyclising said extended linear conotoxin peptide, and

(iv) oxidizing said cyclised peptide to form disulphide bonds.

12. (Once Amended) A process for preparing a cyclic conotoxin according to claim 1 comprising:

(i) synthesizing an extended linear conotoxin peptide on a solid phase support, said extended linear conotoxin peptide comprising a linear conotoxin peptide having a linker moiety attached to at least one end thereof,

(ii) cleaving said linear peptide from the solid support,

(iii) subjecting said extended peptide to conditions such that the peptide folds and forms the required disulphide bonds, and

(iv) cyclising the folded peptide.

13. (Once Amended) A process for preparing a cyclic conotoxin according to claim 1 comprising:

(i) reacting a conotoxin peptide with a linker moiety to form an extended linear conotoxin peptide having said linker moiety attached to one end thereof, and



(ii) cyclising said extended peptide and oxidizing to form disulphide bonds, if required.

14. (Once Amended) Use of a cyclic conotoxin peptide according to claim 1 having activity at ion channel receptors as a neuropharmacological probe.

15. (Once Amended) A method for the treatment or prophylaxis of conditions or diseases in mammals including the step of administering a cyclic conotoxin peptide according to claim 1.

16. (Once Amended) Use of a cyclic conotoxin peptide according to claim 1 in the manufacture of a medicament for the treatment or prophylaxis of diseases or conditions of mammals.

17. (Once Amended) A composition comprising a cyclic conotoxin peptide according to claim 1 and a pharmaceutically acceptable carrier or diluent.

18. A composition according to claim 17 which is pharmaceutical composition.